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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Eran Blaugrund et al.
Serial No. : 10/712,958
Filed : November 13, 2003
For : USE OF RASAGILINE WITH OR WITHOUT RILUZOLE TO
TREAT AMYOTROPHIC LATERAL SCLEROSIS

1185 Avenue of the Americas
New York, New York 10036
September 7, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following documents which are listed on Form PTO-1449 (**Exhibit A**) and are also listed below.

Pursuant to the Notice appearing in the August 5, 2003 Official Gazette, because this application was filed after June 30, 2003, copies of the U.S. Patents and U.S. Patent Application Publications listed herein are not provided.

This Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3) before the mailing of a first Office Action on the merits. Thus, this Information Disclosure Statement should be entered and considered. Copies of the documents listed below as items 14-37 are attached hereto as

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Exhibits 1-21. A copy of items 33, 34 and 36 will be forwarded in due course.

Items 16 and 27 below were cited in the June 16, 2004 International Search Report issued in Connection with PCT International Application No. PCT/US03/36288 which is related to the subject application. A copy of the International Search Report is enclosed as **Exhibit B**.

1. U.S. Patent No. 5,387,612, issued February 7, 1995 to Youdim, et al.;
2. U.S. Patent No. 5,453,446, issued September 26, 1995 to Youdim, et al.;
3. U.S. Patent No. 5,457,133, issued October 10, 1995 to Youdim, et al.;
4. U.S. Patent No. 5,668,181, issued September 16, 1997 to Youdim, et al.;
5. U.S. Patent No. 5,576,353, issued November 19, 1996 to Youdim, et al.;
6. U.S. Patent No. 5,532,415, issued July 2, 1996 to Youdim, et al.;

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7. U.S. Patent No. 5,599,991, issued February 4, 1997 to Youdim, et al.;
8. U.S. Patent No. 5,786,390, issued July 28, 1998 to Youdim, et al.;
9. U.S. Patent No. 5,519,061, issued May 21, 1996 to Youdim, et al.;
10. U.S. Patent No. 5,891,923, issued April 6, 1999 to Youdim, et al.;
11. U.S. Patent No. 5,744,500, issued April 28, 1998 to Youdim, et al.;
12. U.S. Patent No. 6,316,504, issued February 7, 1995 to Youdim, et al.;
13. U.S. Patent Application Publication No. 2004/0010038 A1, published on January 15, 2004;
14. PCT International Application No. PCT/US03/05871 filed February 27, 2003, International Publication No. WO 2003/072055 A2 published September 4, 2003 (**Exhibit 1**);
15. PCT International Application No. PCT/US03/036288 filed November 13, 2003, International Publication No. WO 2004/045515 A2 published June 3, 2004 (**Exhibit 2**);

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16. Bensimon G, et al., (1994) A controlled trial of riluzole in amyotrophic lateral sclerosis. ALS/Riluzole Study Group. N Engl J Med., 330(9):585-91 (**Exhibit 3**)
17. Bentué-Ferrer D, et al., (1996) Monoamine Oxidase B Inhibitors. CNS Drugs., 6(3):217-36 (**Exhibit 4**)
18. Doble A. (1996) The pharmacology and mechanism of action riluzole. Neurology, 47 (Suppl. 1):S233-41 (**Exhibit 5**);
19. Eliash S, et al. (2001) "Rasagiline and its (S) enantiomer increase survival and prevent stroke in salt-loaded stroke-prone spontaneously hypertensive rats. J. Neural Transm., 108:909-23 (**Exhibit 6**);
20. Ferrante RJ, et al., (1997) Increased 3-nitrotyrosine and oxidative damage in mice with a human copper/zinc superoxide dismutase mutation. Ann. Neurol., 42:326-34 (**Exhibit 7**);
21. "Guidance for Industry: *In vivo* drug metabolism/drug interaction studies - study design, data analysis, and recommendations for dosing and labeling," U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), November 1999 (**Exhibit 8**);

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22. Gurney ME, et al., (1994) Motor neuron degeneration in mice that express a human superoxide dismutase mutation. Science, 264:1772-5 (**Exhibit 9**);
23. Gurney ME, et al., (1996) Benefit of vitamin E, riluzole, and gabapentin in a transgenic model of familial amyotrophic lateral sclerosis. Ann. Neurol., 39:147-57 (**Exhibit 10**);
24. Huang W, et al., (1999) Neuroprotective effect of rasagiline, a selective monoamine oxidase-B inhibitor, against closed head injury in the mouse. Eur. J. Pharmacol., 336:127-35 (**Exhibit 11**);
25. Kong J, et al., (1998) Massive mitochondrial degeneration in motor neurons triggers the onset of amyotrophic lateral sclerosis in mice expressing a mutant SOD1. J. Neurosci., 18:3241-50 (**Exhibit 12**);
26. Lacomblez L, et al., (1996) Dose-ranging study of riluzole in amyotrophic lateral sclerosis. Lancet, 347:1425-31 (**Exhibit 13**);
27. Lange DJ, et al., (1998) Selegiline is ineffective in a collaborative double-blind, placebo-controlled trial for treatment of amyotrophic lateral sclerosis. Arch Neurol., 55(1):93-6 (**Exhibit 14**);

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28. Ludolph AC, et al., (1999) Antiglutamate therapy in ALS - which is the next step? J. Neural Transm., 55(Suppl.):79-96 (**Exhibit 15**);
29. Maruyama W, et al., (2000) Neurotoxins induce apoptosis in dopamine neurons: protection by N-propargylamine-1(R)- and (S)-aminoindan, rasagiline and TV1022. J. Neural Transm., 60(Suppl):171-86. (**Exhibit 16**);
30. Maruyama W, et al. (2001) Transfection-enforced bcl-2 overexpression and an anti-Parkinson drug, rasagiline, prevent nuclear accumulation of glyceraldehyde-3-phosphate dehydrogenase induced by an endogenous dopaminergic neurotoxin, N-methyl(R)salsolinol. J. Neurochem., 78:727-35 (**Exhibit 17**);
31. Physicians Desk Reference (2002), p. 772-5 (**Exhibit 18**)
32. Speiser Z, et al., (1999) Studies with rasagiline, a monamine oxidase-B inhibitor, in experimental focal ischemia in the rat. J. Neural Transm., 106:593-606 (**Exhibit 19**);
33. Traynor BJ, et al., (2001) Riluzole and prognosis in amyotrophic lateral sclerosis: Findings of the Irish amyotrophic lateral sclerosis register over a five year study period 1995-2000. ALS and Other Motor Neuron Disorders, 2(Suppl. 2):43-4;

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34. Turner MR, et al., (2001) The King's data base 1990-2000: An analysis of the effect on survival of interventions in ALS. ALS and Other Motor Neuron Disorders, 2(Suppl. 2):43;
35. Vielhaber S, et al., (2000) Mitochondrial DNA abnormalities in skeletal muscle patients with sporadic amyotrophic lateral sclerosis. Brain, 123:1339-48 (**Exhibit 20**);
36. Wong PC, et al., (1995) An adverse property of a familial ALS-linked SOD1 mutation causes motor neuron diseases characterized by vacuolar degeneration of mitochondria. Neuron, 14:1105-16; and
37. Youdim MBH, et al., (2001) Rasagiline (N-propargyl-1R(+)-aminoindan), a selective and potent inhibitor of mitochondrial monoamine oxidase B. Br. J. Pharmacol., 132:500-6 (**Exhibit 21**).

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

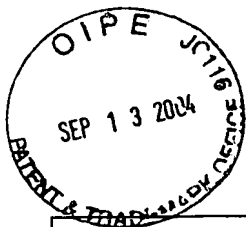
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Pursuant to 37 C.F.R. §1.97(b), no fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	
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Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. 67705/JPW/GJG/MML		Serial No. 10/772,958							
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				Applicants: Eran Blaugrund et al.									
				Filing Date November 13, 2003		Group							
U.S. PATENT DOCUMENTS													
Examiner Initial		Document Number						Date	Name	Class	Subclass	Filing Date if Appropriate	
		5	3	8	7	6	1	2	2/7/95	Youdim, et al.			
		5	4	5	3	4	4	6	9/26/95	Youdim, et al.;			
		5	4	5	7	1	3	3	10/10/95	Youdim, et al.;			
		5	6	6	8	1	8	1	9/16/97	Youdim, et al.;			
		5	5	7	6	3	5	3	11/19/96	Youdim, et al.;			
		5	5	3	2	4	1	5	7/2/96	Youdim, et al.;			
		5	5	9	9	9	9	1	2/4/97	Youdim, et al.;			
		5	7	8	6	3	9	0	7/28/98	Youdim, et al.;			
		5	5	1	9	0	6	1	5/21/96	Youdim, et al.;			
		5	8	9	1	9	2	3	4/6/99	Youdim, et al.;			
		5	7	4	4	5	0	0	4/28/98	Youdim, et al.;			
		6	3	1	6	5	0	4	2/7/95	Youdim, et al.;			
		20	04	00	10	0	3	8	1/15/04	Blaugrund et al.;			
FOREIGN PATENT DOCUMENTS													
		Document Number						Date	Country	Class	Subclass	Translation Yes No	
		WO	20	03	07	2	0	5	5	9/4/2003	PCT;		
		WO	20	04	04	5	5	1	5	6/3/04	PCT;		
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)													
		Bensimon G, et al., (1994) A controlled trial of riluzole in amyotrophic lateral sclerosis. ALS/Riluzole Study Group. <u>N Engl J Med.</u> , 330(9):585-91;											
		Bentué-Ferrer D, et al., (1996) Monoamine Oxidase B Inhibitors. <u>CNS Drugs.</u> , 6(3):217-36;											
		Doble A. (1996) The pharmacology and mechanism of action riluzole. <u>Neurology</u> , 47 (Suppl. 1):S233-41;											
		Eliash S, et al. (2001) "Rasagiline and its (S) enantiomer increase survival and prevent stroke in salt-loaded stroke-prone spontaneously hypertensive rats. <u>J. Neural Transm.</u> , 108:909-23;											
		Ferrante RJ, et al., (1997) Increased 3-nitrotyrosine and oxidative damage in mice with a human copper/zinc superoxide dismutase mutation. <u>Ann. Neurol.</u> , 42:326-34;											
		"Guidance for Industry: <i>In vivo</i> drug metabolism/drug interaction studies – study design, data analysis, and recommendations for dosing and labeling," U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), November 1999;											
		Gurney ME, et al., (1994) Motor neuron degeneration in mice that express a human superoxide dismutase mutation. <u>Science</u> , 264:1772-5;											
EXAMINER		DATE CONSIDERED											
*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.													

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Exhibit A

